United States Court of Appeals

for the Second Circuit

APPELLANT'S BRIEF

74-2477

UNITED STATES COURT OF APPEALS

FOR THE SECOND CIRCUIT

B

P/S

STERLING DRUG INC., WINTHROP PRODUCTS, INC. and BREON LABORATORIES, INC.,

Plaintiffs-Appellants,

- against -

CASPAR W. WEINBERGER, Secretary of Health, Education and Welfare, and ALEXANDER M. SCHMIDT, Commissioner of Food and Drugs,

Defendants-Appellees.

BRIEF OF PLAINTIFFS-APPELLANTS

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The Issues Presented

1. Where plaintiffs fully participated in the administrative process and appealed to this Court from an

adverse determination therein, and where, on appeal, the Court found that defendants formally abandoned the position they had adopted in the order appealed from, are defendants barred from again raising that exact contention in a new proceeding involving the same parties and same product?

2. Where plaintiffs' pharmaceutical product has been lawfully marketed for over twenty years as a "single entity" drug, may defendants institute a proceeding to withdraw approval of the new drug applications for that drug on the grounds that it may be viewed as a "fixed combination" drug, when defendants' notice fails to specify, and, in fact, defendants do not possess any "new information" as required by statute which would indicate that the drug is a "fixed combination" product and that it is ineffective as such?

3. Where defendants' new proposal to withdraw approval of the new-drug applications for plaintiffs' pharmaceutical product is, on the one hand, barred by res judicata and related doctrines, and, on the other hand, without statutory basis, must plaintiffs participate in the administrative process and raise these issues in the first instance before the administrative agency?

STATEMENT OF THE CASE

On September 30, 1974, plaintiffs commenced this action in the United States District Court for the Southern District of New York. The verified Complaint (A 4-54) sought a declaratory judgment declaring that a proposal of the Food and Drug Administration ("FDA") to withdraw approval of the new-drug applications ("NDA's") for plaintiffs' pharmaceutical product, Alevaire, was (a) barred in part by the doctrines of res judicata and/or collateral estoppel and estoppel by admission and abandonment as a result of prior proceedings in this Court which culminated in a decision dated May 2, 1973 in dockets 73-1628 and 2481; and (b) illegal in remaining part since defendants lacked the "new information" required by statute before such a proceeding could be commenced, Section 505(e)(3) of the Federal Food, Drug, and Cosmetic Act, ("the Act"), 21 U.S.C. §355(e), (Addendum A hereto).

Jurisdiction exists under the United States Constitution, Amendment V; the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §301 et seq.; the Administrative Procedure Act, 5 U.S.C. §551 et seq.; and 28 U.S.C. §§1331, 1332, 1337, 1651, 2201 and 2202.

Plaintiffs also sought a preliminary and permanent

injunction enjoining defendants from proceeding with their new proposal. By order to show cause dated October 1, 1974, plaintiffs' motion for a preliminary injunction was made returnable on October 10, 1974 before the Honorable Lawrence W. Pierce, U.S.D.J. (A 55).

On October 10, 1974 a hearing was held before Judge Pierce and, at the suggestion of the Court, the motion for a preliminary injunction was consolidated with trial on the merits pursuant to Rule 65(a)(2), Fed.R.Civ.P. (A 157-158). Plaintiffs requested the opportunity to present the testimony of three witnesses at the hearing, but actual testimony was not necessary since defendants stipulated as to the testimony the witnesses would offer, without conceding the truth thereof (A 196).

By decision dated and filed October 31, 1974, Judge Pierce ruled that the injunction would be denied and the Complaint dismissed for failure of plaintiffs to exhaust their administrative remedies (A 197). On November 5, 1974 in the absence of Judge Pierce, an order denying the injunction and dismissing the Complaint was signed by Judge Gagliardi (A 227), and on November 6, 1974, said order was entered by the Clerk of the District Court and plaintiffs filed a Notice of Appeal therefrom (A 228).

Also, on November 6, 1974, plaintiffs moved in this Court (since Judge Pierce was out of the country) for an injunction pending appeal, since in the absence of such relief, plaintiffs would have been required to make a full submission in the administrative proceeding on November 15, 1974. On November 12, 1974, plaintiffs' motion for an injunction was heard, and this Court directed that the appeal be expedited and set for argument the week of December 16, 1974. The administrative process was stayed pending oral argument of the appeal. The parties were also given permission to file typewritten briefs.

STATEMENT OF FACTS

Alevaire is a prescription drug which has been available in this country and abroad since 1952 when the FDA first approved NDA's for the drug. Alevaire is a muco-evacuant agent containing the detergent or surface active agent, tyloxapol, in an aqueous vehicle containing sodium bicarbonate and glycerin. It is aerosolized and administered by inhalation to patients with chronic obstructive lung diseases accompanied or complicated by excessive or thickened broncho-pulmonary secretions.

The present controversy has its genesis in proceedings which commenced in July 1968, when the FDA, based on a report of a panel of the National Academy of Science - National

Research Council ("NAS-NRC"), first offered its opinion that there was a lack of substantial evidence, (as defined by the 1962 Amendments to the Act), that Alevaire was effective for its labeled indications (A 59; 159).

The history of the proceedings which then ensued is recited in the decision below (A 197-209) and in the opinion of this Court in dockets 73-1628 and 2481 (A 37-52). We will recite here the relevant highlights.

The NAS-NRC Report and FDA's Concurrence Therein

The NAS-NRC panel which reviewed Alevaire clearly considered it to be a "single entity" drug, i.e., a drug with one active ingredient. The active ingredient in Alevaire is the detergent or surface active agent, tyloxapol. The entire text of the panel report is as follows:

> "COMMENTS: This detergent for inhalation by aerosol is marketed in a concentration of 0.125%. Thus, over 90% of the material is water. It has been shown in vitro that tyloxapol in higher concentration can affect certain physical characteristics of mucus (20). There is no evidence that the tyloxapol in this product has any effect on secretions in the lung other than that of water in thinning secretions by simple dilution (1,13,22).
>
> "It should be noted that a number of the papers in the manufacturer's bibliography

> are based only on clinical impression and do not reflect adequate controls. The clinical impression of the Panel is that this product is no more effective than water." (A 59).

In July 1968, plaintiffs were notified of this report and of the FDA's concurrence therein. Specifically, the FDA stated it concurred in the panel's conclusion that "there is no evidence that tyloxapol ... in the amount present ... has any effect on secretions in the lung other than that of water in thinning secretions by simple dilution." (A 39; 69). Plaintiffs promptly arranged for clinical studies to be conducted to test the effectiveness of the drug, and, in August 1968, they informed the Agency that the studies would compare the effectiveness of Alevaire against water and saline (A 48).

The First Withdrawal Order - August, 1971

In June 1970, the studies, which had been conducted by Drs. Miller and Paez of the University of Texas Southwestern Medical School ("the Miller-Paez study") and by Dr. Cohen of the New Jersey College of Medicine and Dentistry ("the Cohen study"), were submitted to the FDA along with a full complement of supporting data. Shortly thereafter, plaintiffs also submitted affidavits from numerous independent experts who had

reviewed the studies, found them to be adequate and well-controlled, and found them to prove the effectiveness of Alevaire (A 41).

In submitting the material, plaintiffs sought either to convince the FDA that Alevaire was effective and that the proceeding should be terminated, or to have the FDA convene an evidentiary hearing pursuant to Section 505(e) of the Act, 21 U.S.C. §355(e) (Addendum A hereto), at which the evidence could be reviewed in depth. However, by order dated August 27, 1971, the FDA rejected the Miller-Paez and Cohen studies as being inadequate and uncontrolled, denied plaintiffs an evidentiary hearing and ordered the withdrawal of approval of the NDA's for Alevaire (A 17).

Plaintiffs appealed to this Court in Docket 71-1898 and in due course filed their printed briefs and appendix. Shortly thereafter, the FDA, conceding that it had failed to consider relevant material in plaintiffs' submissions, moved for permission to revoke its withdrawal order and to remand the matter to the Agency for futher consideration (A 41). In anticipation of a prompt review, the motion was granted in January 1972.

The Second Withdrawal Order - March, 1973

Over a year later, in March 1973, the FDA issued a second withdrawal order. In this order, the Agency again found

the Miller-Paez and Cohen studies to be inadequate and uncontrolled and denied plaintiffs' request for an evidentiary hearing. The principal ground stated in the order for rejecting the studies was that Alevaire was a single entity drug which:

> "must be compared to its own vehicle, in other words, to a product containing the ingredients of Alevaire minus tyloxapol, i.e, a solution of 2 percent sodium bicarbonate, 5 percent glycerin and 93 percent water." (A 23).

This ground had not appeared in the first withdrawal order. Indeed in that order, the Agency had admitted that water was an appropriate control (A 42).

Plaintiffs promptly assembled and filed with the Agency a Petition for Reconsideration, which was supported by the affidavits of four experts (A 42). In these affidavits, the experts rebutted point by point each criticism of the Miller-Paez and Cohen studies and especially refuted the principal critique raised by FDA, namely, that the effectiveness of Alevaire could only be tested by comparing Alevaire to its vehicle, i.e., Alevaire minus tyloxapol. For example, Dr. Donald Egan, Director of Pulmonary Medicine

at New Britain General Hospital and author of the text Fundamentals of Respiratory Therapy, stated:

> "The order rejects the two studies on the grounds that the only proper control would be a solution consisting of 2 percent sodium bicarbonate, 5 percent of glycerin and 93 percent water. Since water and saline are two of the most commonly used mucoevacuant agents, it is entirely appropriate to test the effectiveness of Alevaire against them as controls. The solution suggested by FDA as the only proper control is, in fact, merely an alternative which might have been used. (A 62)
>
> "Accordingly, I must strenuously disagree with FDA's conclusion that 'to establish effectiveness, the studies relied on would have to at least compare Alevaire to a product containing an aqueous solution of 2 percent sodium bicarbonate and 5 percent glycerin.'" (Affidavit of Donald F. Egan, M.D., ¶¶ 4-5).

Similarly, Dr. Thomas L. Petty, Professor of Medicine and Head of the Division of Pulmonary Diseases at the University of Colorado School of Medicine and Medical Center stated:

> "I am also disturbed at the repeated comment that the only proper control would be a solution of 2 percent sodium bicarbonate, 5 percent glycerin and 93 percent water, that is, Alevaire minus tyloxapol. I do not agree that using this as a control is a proper study design

and believe that a more inert control such as water and saline is far more preferable." (Affidavit of Thomas L. Petty, M.D., ¶6). (A 62)

Despite these and other comments demonstrating that the March 1973 order was scientifically untenable, the FDA was unwilling even to grant plaintiffs an evidentiary hearing. It informed plaintiffs that the Petition for Reconsideration would be denied and plaintiffs again appealed to this Court (A 42; 62-63).

The Third Withdrawal Order - August, 1973

Then, suddenly, the FDA again reversed ground. Unilaterally, it issued a notice which terminated its March 1973 order and reinstated approval of the NDA's (A 25). At the same time, it moved to dismiss the pending appeal on the grounds that it was moot. Plaintiffs opposed that motion, and, while the motion was pending, FDA issued a third order on August 7, 1973 denying a hearing and withdrawing approval of the NDA's for Alevaire (A 26). The sole ground supporting this new order was the contention, never before raised in the proceedings, that Alevaire was a "fixed combination" drug within the meaning of 21 CFR 3.86 for which there must be proof of effectiveness of each of the ingredients against each other, namely, tyloxapol, sodium bicarbonate, glycerin and water.

This Court thereafter denied defendants' motion to dismiss the appeal from the March 1973 order as moot, and, when plaintiffs appealed from the August 1973 order as well, the two appeals were consolidated for review (A 43).

Proceedings Before this Court

In their brief on appeal from the March 1973 order, plaintiffs noted that the August 1973 order had, in effect, abandoned all criticisms of the Miller-Paez and Cohen studies. We stated:

> "Although this Court rejected FDA's attempt to substitute the third order, it is pertinent in considering the March order since it concedes the validity of petitioners' comments made in the Petition for Reconsideration. FDA stated [in its August 1973 order]:
>
> > 'In the petition for reconsideration ... the NDA holders took issue with every facet of the evaluations of the Miller-Paez and Cohen studies contained in [the March] notice.
> >
> > 'The commissioner finds that certain criticisms delineated in the petition are well founded when the investigations are accepted at face value as is required in the ruling upon the adequacy of a request for hearing under 21 CFR 130.12(a)(5) and 130.14. However, the Commissioner also finds that

> another analysis of these two studies, which would take into account the several valid objections made in the petition for reconsideration would be a meaningless and unnecessary endeavor.'
>
> "Thus, FDA comes before this Court having conceded the inaccuracy of several of its prior criticisms of the two studies, but having failed to explain the precise grounds on which it would reject the studies ... On the record now before this Court, there are the affidavits of Drs. Beck, Cohen, Collins, Egan, Head, Miller, Petty, Ravenel, Schools and Texter that the studies are adequate and well-controlled and establish the effectiveness of Alevaire. There is absolutely no evidence to the contrary." Pl. Br. in Docket 73-1628, p. 18.

In their answering brief, defendants made clear that the only reason then claimed for rejecting the Miller-Paez and Cohen studies was that they failed to isolate the effectiveness of <u>each</u> ingredient, i.e., that they were not relevant to the fixed combination theory. Thus, defendants stated:

> "The essential findings on the Miller-Paez and Cohen data may be summarized as follows:
>
> "1. The petition for reconsideration did contain several valid criticisms when the studies are analyzed at face value, as the respondents' regulations require.

"2. A new evaluation to show why the data are not well-controlled is irrelevant since the design of the studies does not allow assessments respecting the contribution each of the three components of Alevaire makes to the claimed effectiveness of Alevaire.

"3. Alevaire is a combination of three components in water: 0.125 percent tyloxapol, with 2 percent sodium bicarbonate and 5 percent glycerin. Since 1953 the labeling of Alevaire has claimed that each of the three components contribute to the claimed effectiveness of the drug.

"4. The Miller-Paez and Cohen studies were comparisons of Alevaire with water and/or saline and accordingly could not show what contribution to the total effectiveness of the drug each of the three components made." (Def. Brief in Dockets 73-1628 and 2481, pp. 6-7; cites omitted).

In their reply brief, plaintiffs then highlighted to the Court that defendants had failed and refused to identify any reason why the Miller-Paez and Cohen studies were inadequate or uncontrolled. Under the argument heading:

"The Government Has Failed to Show that the Miller-Paez and Cohen Studies, Which Establish the Effectiveness of Alevaire, Are Inadequate or Uncontrolled"

we wrote:

"Perhaps the most remarkable feature of respondents' brief is its failure to

> deal on the merits with the Miller-Paez and Cohen studies ... Instead, FDA argues, with the zeal typical of a recent convert, that Alevaire is a fixed-combination drug and that petitioners' studies are irrelevant since they fail to test the comparative effectiveness of each ingredient in Alevaire." (Pl. Reply Br., pp. 2-3).*

With the issues thus posed, oral argument was heard before this Court on February 1, 1974. As the record below indicates (A 196-197), in response to a direct inquiry from the Bench, counsel for defendants abandoned any remaining (although unstated) criticisms of the studies and unequivocally stated that the FDA no longer objected to the Miller-Paez and Cohen studies as inadequate or uncontrolled, but argued only that they were unresponsive to the fixed combination theory.

The Decision of this Court

On May 2, 1974 this Court rendered its decision on the prior appeals (A 36). It noted that the third order of August 7, 1973, "abandoned the grounds on which the prior two orders of March 2, 1973 and August 27, 1971 had been based", cited defendants' confession of error with regard to the March 1973 order, and referred to that order as "concededly erroneous." However, since the March order had already been

*Plaintiffs below sought to introduce the prior briefs and appendix as part of the record in this case, but Judge Pierce rejected that offer, although agreeing that reference could be made to them (A 158; 171).

revoked by the FDA, which had also reinstated approval of the NDA's, the Court stated: "We fail to see what relief could be granted to petitioners under these circumstances." Accordingly, it dismissed the appeal from the March 1973 order as moot in the belief that the relief sought by plaintiffs had already been achieved.

With regard to the August 1973 order, the Court noted that the fixed combination theory contained therein surfaced only after the Supreme Court's decision in Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609 (1973), wherein the Supreme Court had affirmed an order directing the FDA to hold an evidentiary hearing on a proposed NDA withdrawal (A 47-48). This Court further stated that there was "little in the record now before us to support the proposition that Alevaire is a fixed combination drug within the meaning of 21 CFR 3.86 ..." (A 52). It then set aside the August order for lack of notice and warned that if the FDA wished to proceed again on the fixed combination ground, "it must follow the procedure required in the statute and regulations." (A 52).

Defendants' New Proposal - The Notice of August, 1974

By notice dated August 1, 1974 and published in the Federal Register of August 13, 1974, the FDA issued a new proposal to withdraw approval of the NDA's for Alevaire (A 53). As might have been anticipated given the history of these proceedings, the new proposal is ambiguous and inconsistent with past pronouncements by the Agency.

For example, in its August 1973 order and in its appearance before this Court on the prior appeal, FDA had made it quite clear that it had finally concluded that Alevaire was a fixed combination drug. However, in the new proposal, it announced that Alevaire could be viewed as either a "single entity" drug containing one active ingredient, tyloxapol, or as a fixed combination drug containing three active ingredients, tyloxapol, sodium bicarbonate and water. Even viewing Alevaire as a fixed combination product, FDA has obviously withdrawn from the position it took in the August 1973 order. There, it contended that glycerin was an active ingredient the effect of which would have to be isolated by comparative testing. In the new proposal, it concedes that "glycerin, apparently intended to affect aerosol droplet size, could be added to all [control] groups."

According to the new proposal, if Alevaire is a single entity drug, then its effectiveness must be tested by comparing Alevaire to its vehicle, namely, Alevaire minus tyloxapol. This, of course, is the precise contention raised in the March 1973 order and rebutted by plaintiffs in their Petition for Reconsideration which this Court described as "an extensive rebuttal ... which, in the light of subsequent events, was apparently well taken." (A 42). The "subsequent events" were defendants' eventual complete abandonment of this position during the course of the prior appeal.

The new proposal fails to specify what "new information" defendants possess to satisfy the requirements of Section 505(e)(3) of the Act, 21 U.S.C. §355(e)(3). However, the record below now demonstrates that defendants rely on the 1968 NAS-NRC report as supplying the "new information" to support the entire proposal (A 122; 126). But, it is apparent from the face of the panel report, and from the Agency's interpretation of that report from its issuance up until August 1973, that the NAS-NRC panel viewed Alevaire as a single entity drug, the active ingredient of which is tyloxapol. There is simply no reference in the panel report to Alevaire as being, or even possibly being, a fixed combination product, and no other "new information" is relied upon by the Agency to support its proposal.

The Damage Incurred By Plaintiffs During these Proceedings

The record reflects that since 1968 the FDA has issued numerous public pronouncements that Alevaire is ineffective and it has continued to maintain Alevaire on a widely circulated list of "ineffective" drugs which prohibits its purchase by government agencies and prohibits the use of federal funds to reimburse its purchase by state or local governments, private hospitals or individual patients.

Yet, the fact remains that the defendants have been unable to justify their public pronouncements. Twice, the FDA

was forced to abandon its own final orders herein and its third attempt was set aside by this Court.

Despite the arbitrary conduct of defendants and their inability to support their opinions, their repeated public pronouncements have had a chilling effect on the reputation of Alevaire among the medical profession and have occasioned a loss of sales of approximately 65% since 1968 (A 67).

ARGUMENT

Summary of Argument

In its decision of May 2, 1974 this Court found that in the prior proceedings with respect to Alevaire the FDA raised and then abandoned and conceded to be erroneous the theory that Alevaire must be tested by comparing it to its vehicle. The FDA is, therefore, barred by res judicata, collateral estoppel, and estoppel by admission and abandonment from again raising that issue in its new proposal to withdraw approval of plaintiffs' NDA's.

FDA's contention in its new proposal that Alevaire is a fixed combination drug is also not sustainable as a ground for proceeding to withdraw approval of the NDA's for Alevaire, because the FDA lacks the "new information" required by statute to support that contention. Thus its new pro-

ceeding, insofar as it is based on the fixed combination contention, is in clear violation of a statutory prerequisite.

There are only two grounds upon which the FDA's new proposal is based. The single entity ground cannot result in a valid final order since defendants are barred from again contending that Alevaire must be tested against its vehicle. The fixed combination ground lacks proper statutory foundation. Accordingly, plaintiffs are entitled to relief enjoining such an illegal and invalid proceeding and are not required to proceed once again through the administrative process.

Therefore, the judgment of the District Court should be reversed.

POINT I

DEFENDANTS ARE BARRED BY RES JUDICATA, COLLATERAL ESTOPPEL AND ESTOPPEL BY ADMISSION AND ABANDONMENT FROM PROCEEDING TO WITHDRAW APPROVAL OF PLAINTIFFS' NDA's FOR ALEVAIRE ON THE GROUND THAT THE EFFECTIVENESS OF THE DRUG CAN ONLY BE ESTABLISHED BY TESTS COMPARING IT WITH ITS VEHICLE SOLUTION

1. Defendants' Explicit Concessions as Reflected in this Court's Prior Decision Preclude Relitigation of the Issue of Whether Alevaire Must Be Tested Against its Vehicle.

A. Res Judicata and Collateral Estoppel Bar the New Proposal

It is apparent that defendants' new Notice, insofar as it considers Alevaire to be a single-entity drug, is barred

by the decision of this Court of May 2, 1974, which is based in pertinent part on the concessions and admissions made by defendants in the prior proceeding. In their new Notice, defendants again contend, as they did in their March 1973 order, that Alevaire must be compared to its own vehicle. Thus, the new Notice states:

> "If Alevaire is a single active component in a several component vehicle, the required clinical studies are somewhat less complex. In this case evidence must be presented that Alevaire is more effective than its admittedly active vehicle. Development of such evidence would require a two-group trial: patients treated with the vehicle (water, bicarbonate, and glycerin) alone vs. patients treated with Alevaire." (A 53).

This is precisely the proposal which was included in FDA's second withdrawal order in March 1973 (A 20); rebutted by plaintiffs' Petition for Reconsideration and by the sworn statements of independent experts in the field submitted to FDA by plaintiffs (A 42); and found by this Court to have been abandoned by FDA in its third withdrawal order in August 1973 (A 26) and in its previous briefs and argument before this Court (A 43).

There can be no question that the issue raised in defendants' new proposal is precisely the ground raised in the March 1973 order wherein, as this Court noted in its May 2, 1974 decision:

> "[T]he criticism was also voiced that water was not a proper 'control' with which to compare Alevaire, but that the proper 'control' was Alevaire minus tyloxapol.[6]

---

[6]In other words, a solution of 2% sodium bicarbonate, 5% glycerine and 93% water. The FDA had previously suggested that either water or Alevaire minus tyloxapol would be a proper 'control'." (A 42).

The Court also noted that plaintiffs then submitted "an extensive rebuttal of the grounds on which the order was based, which in the light of subsequent events, was apparently well taken", explaining that this rebuttal "included material supporting the suitability of the controls used in petitioners' clinical studies under 21 C.F.R. 130.12(a)(5)(ii)(a)(4)(iii)." (A 42). The Court found that the FDA's third order "abandoned the grounds on which the prior two orders of March 2, 1973 and August 27, 1971 had been based," (A 43) and that defendants in their brief "confessed error in that order [of March 2, 1973]." The Court also described the March order as "concededly erroneous." (A 44)*

If the language of the decision leaves any doubt as to what was abandoned by the FDA, the unrebutted record herein

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*Later in the opinion the Court reiterated that:

> "Until August, 1973 ... the objection to petitioners' submission raised by the FDA was that the studies were not 'adequate and well-controlled'. Both of the prior withdrawal orders, of August 27, 1971 and March 2, 1973, which the FDA itself terminated after they had been appealed from, were predicated on that ground." (A 48).

reflects that on oral argument of the appeals, counsel for defendants explicitly stated that the Agency no longer objected to the Miller-Paez and Cohen studies as inadequate or uncontrolled; but only contended that they were irrelevant to the fixed combination issue (A 64; 196; 214-215).

This concession confirmed what had been the clear impact of the August withdrawal order - that the FDA was not prepared to defend its criticisms of the Miller-Paez and Cohen studies at an evidentiary hearing, as required by the Supreme Court's decision in the Hynson case. And it removed any vestige of legitimacy to the FDA's vague and wholly unsubstantiated allusion in its August order to the existence of some unspecified criticisms of the Miller-Paez and Cohen studies.

Since the FDA's contention had been that the Miller-Paez and Cohen studies were not adequately controlled because water and saline were not proper controls, the concession also constituted a withdrawal of that contention.*

In sum, the abandonment which the Court found to exist was an abandonment of the exact contention now raised again in the new proposal. Accordingly, the Agency has had its day in Court on this issue. Plaintiffs were fully prepared

*As the Court noted, the FDA had previously suggested that water was an appropriate control (A 42).

to proceed to an administrative hearing on the issues posed and had, in fact, requested such relief . Were it not for the Agency's own admissions and concessions, such relief would have been required under Weinberger v. Hynson, Westcott & Dunning, Inc., supra (A 47-48).

Thus, while we do not contend that this Court found Alevaire to be effective or the Miller-Paez and Cohen studies to be adequate and well-controlled, we do contend that this Court found that defendants abandoned its position on those issues on the merits.

There must come an end to an administrative agency's efforts to continue to raise issues which it has previously raised and abandoned, conceding them to be erroneous. The Supreme Court in United States v. Utah Construction & Mining Co., 384 U.S. 394, 422 (1966), stated:

> "When an administrative agency is acting in a judicial capacity and resolves disputed issues of fact before it which the parties have had an adequate opportunity to litigate, the courts have not hesitated to apply res judicata to enforce repose."

This statement was recently cited by this Court in Hudson River Fishermen's Ass'n v. Federal Power Commission, 498 F.2d 827, 834 (2d Cir. 1974).

It is, of course, the fundamental and long-established purpose of the doctrines of res judicata and collateral estoppel to insure repose and to prevent vexation of the parties. Thomas v. Consolidation Coal Co., 380 F.2d 69.77 (4th Cir. 1967), cert. denied 389 U.S. 1004 (1967). Accordingly, the doctrines extend not only to issues actually litigated, but

even to those which might have been litigated had they not been abandoned. As the Supreme Court has stated:

> "The effect of a judgment or a decree as res judicata depends upon whether the second action or suit is the same or a different cause of action. If upon the same cause of action, the judgment or decree upon the merits in the first case is an absolute bar to the subsequent action or suit between the same parties or those in privity with them, not only in respect of every matter which was actually offered and received to sustain the demand, but also as to every ground of recovery which might have been presented." (Emphasis added) Baltimore S.S. Co. v. Phillips, 274 U.S. 316, 319 (1927) Cf., Hudson River Fishermen's Ass'n v. Federal Power Commission, supra, where res judicata was not applied only because, in contrast to the case at bar, there had not been an opportunity to litigate an issue.

Whether the present proceeding by defendants against plaintiffs be viewed as the same or a different cause of action as the previous proceeding is relevant only insofar as it determines whether the principle applied be technically denominated as res judicata or collateral estoppel. The effect of the principle is the same, since whether by res judicata or collateral estoppel, defendants are barred from again attempting to proceed against plaintiffs on the basis that Alevaire must be compared to its vehicle.

> "[W]here the second action between the same parties is upon a different cause or demand, the principle of res judicata is applied much more narrowly ... Since the cause of action involved in the second pro-

> ceeding is not swallowed by the judgment in the prior suit, the parties are free to litigate points which were not at issue in the first proceeding ... But matters which were actually litigated and determined in the first proceeding cannot later be relitigated. Once a party has fought out a matter in litigation with the other party, he cannot later renew that duel. In this sense, res judicata is usually and more accurately referred to as estoppel by judgment, or collateral estoppel. Commissioner v. Sunnen, 333 U.S. 591, 597-98 (1948).

Here, defendants have not only had the opportunity to litigate the issue, but have themselves raised the issue and then specifically and formally abandoned it after plaintiffs made a full and "well taken" response thereto. (A 42). The Supreme Court has refused to permit agencies to avoid effective appellate review of their actions by issuing short-term orders and then withdrawing them so that they become moot, as the FDA attempted to do here with respect to the March 1973 order. Southern Pacific Terminal Co. v. ICC, 219 U.S. 498 (1911).

Since the issue was before the Agency and this Court, and since the decision of this Court makes it clear that the issue has been concluded in plaintiffs' favor, defendants are estopped from attempting again to raise this issue. Tait v. Western Maryland R. Co., 289 U.S. 620 (1933); Commissioner v. Western Union Tel. Co., 141 F.2d 774 (2d

Cir. 1944), cert. denied 332 U.S. 751 (1944).

In United States v. Willard Tablet Co., 141 F.2d 141 (7th Cir. 1944), the doctrine of res judicata was applied to an attempt by FDA to relitigate an issue of fact that had previously been adjudicated between the government and respondents, even though the government in the earlier proceeding was a different Federal agency, the Federal Trade Commission. Res judicata certainly applies here, therefore, where the FDA itself is the agency involved in both proceedings.

In addition to Willard Tablet, the principles of res judicata and collateral estoppel have been applied against the government in a variety of other situations. Vestal v. Commissioner, 152 F.2d 132 (D.C. Cir. 1945); Chapman v. El Paso Natural Gas Co., 204 F.2d 46 (D.C. Cir. 1953); Nager Electric Co. v. United States, 396 F.2d 977 (Ct. Cl. 1968). After six years and three appeals, the attempt to renew this issue constitutes harassment by defendants which should not be countenanced by this Court. Cover v. Schwartz, 133 F.2d 541 (2d Cir. 1942), cert. denied 319 U.S. 748 (1943).

B. Estoppel By Admission and Abandonment Bar the New Proposal

In addition to the doctrines of res judicata and collateral estoppel, defendants are also estopped from proceeding anew on the previously raised theory since they

formally and specifically, in orders, briefs and on oral argument of counsel, abandoned said contention and conceded it to be erroneous. Cf., KFC National Management Corp. v. N.L.R.B., 497 F.2d 298, 305 (2d Cir. 1974).

There are numerous cases which hold that once a party, including the government, concedes a fact or an issue in the course of a proceeding, it will be bound by the concession. Cover v. Schwartz, supra; Fenix v. Finch, 436 F.2d 831 (8th Cir. 1971); United States v. Commanding Officer, 446 F.2d 124 (8th Cir. 1971); United States ex rel. Huisinga v. Star Construction Co., 186 F.2d 666 (10th Cir. 1951).

In Vestal v. Commissioner, supra at 136-137, the court held:

> "[T]he Commissioner, having made, within the scope of his authority, with full knowledge of all the facts and being fully conscious of the problem involved, an election to collect a tax upon a given transaction upon a stated basis, cannot later be heard to assert another tax upon the same transaction ..."

Similarly, defendants here have also, with full knowledge of the facts and being fully conscious of the problem involved, made an election to abandon the contention that Alevaire should be tested against its vehicle. Thus they cannot now assert that contention again.

This Court should, therefore, enjoin defendants from seeking to relitigate the issue of whether Alevaire

must be tested in comparison with its vehicle solution of water, sodium bicarbonate and glycerin, since that issue was raised and then abandoned by defendants in the prior proceedings concluded by this Court's decision on May 2, 1974.

C. Defendants Cannot Avoid the Effect of Res Judicata, Collateral Estoppel, and Estoppel By Admission and Abandonment Because the Prior Appeal was Technically Dismissed as Moot

Defendants argued below on technical grounds that this Court's decision as to the March 1973 order was not final or on the merits since the appeal from that order was dismissed as moot.

The argument is specious since the defendants themselves, by revoking the March 1973 order and abandoning it as substantively erroneous, caused the matter to become moot. We note that this Court itself denied defendants' initial motion to dismiss the appeal as moot (A 43), and thus preserved its jurisdiction to comment fully on the merits. In its decision, this Court made it clear that the appeal from the March order was moot only because the FDA had already revoked the March order and reinstated approval of the NDA's. Thus, there was no further relief which the Court could grant with respect to that order (A 44).

Where, as here, defendants by their own action in abandoning the grounds asserted in the March order caused the dismissal for mootness, they cannot prevent the application of res judicata or collateral estoppel.

Professor Moore discusses the issue in the context of appellate review of lower court judgments, but the principles are clearly applicable here as well:

> "If the appellant is responsible for the intervening change in the status quo that makes appellate review impossible, it is difficult to see why he should be regarded any differently from a party who, having lost in the trial court, has failed to take his appeal within the time allowed by statute. It would be quite destructive to the principle of judicial finality to put such a litigant in a position to destroy the collateral conclusiveness of a judgment by destroying his own right of appeal ... And the same is true when the appellant, by conceding an issue in the appellate court, renders the case moot. Otherwise, any litigant unsuccessful in the trial court could deprive the judgment of collateral estoppel effect by appealing on two grounds, both necessary if the judgment is to be reversed and then conceding one of them in the appellate court." 1B Moore's Federal Practice, ¶0.416[6], pp. 2327-28 (1974)

These principles were applied by this Court in Cover v. Schwartz, supra, where Judge Frank stated:

> "This case has not become moot because of intervening circumstances over which appellant had no control. ... For appellant, who asserted and tried to show infringement in the court below, so that there was controversy before that court, in this court

> concedes that there is no infringement by defendant, which means that there is now no controversy. Although appellee did not ask for a declaratory judgment on the basis of threatened suits by appellant ... nevertheless dismissal of the suit, as distinguished from dismissal of the appeal, might result in unfairness to appellee by subjecting him to other vexatious actions by appellant. ... We shall, therefore, merely dismiss the appeal, with the consequence that the judgment of invalidity made by the trial court will stand as entered." 133 F.2d at 546-547.

Here, plaintiffs are in the same posture as the appellee in Cover v. Schwartz. Plaintiffs were perfectly willing to litigate the issue of the adequacy of the Miller-Paez and Cohen studies and, in fact, that was the relief they requested from this Court. But, when plaintiffs appealed to the Court of Appeals from FDA's order on those studies, FDA conceded that its analysis of those studies had been erroneous, abandoned the grounds asserted in the March 1973 order as a basis for proceeding against Alevaire, and stated in this Court that the adequacy and well-controlled nature of the Miller-Paez and Cohen studies was no longer an issue being contested by the government (A 42-44; 64; 196). Instead, defendants relied entirely on the fixed combination theory as set forth in their August 1973 withdrawal order.

Accordingly, the entire prior proceeding relating to the March 1973 withdrawal order was terminated by and became merged in the prior decision of this Court. It was not, as the defendants contended below, merely an "unconsummated"

proceeding (A 124). Defendants' new attempt to litigate previously decided issues represents the continued "unfairness to [plaintiffs here] by subjecting [them] to other vexatious action by [the government]" deplored by this Court in Cover v. Schwartz, supra at 547. Cf., Southern Pacific Terminal Co. v. ICC, supra; Electrical Fittings Corp. v. Thomas & Betts Co., 307 U.S. 241 (1939); United States v. Munsingwear, Inc., 340 U.S. 36 (1950). Accordingly, plaintiffs in this action, have, as the Court in Cover v. Schwartz implied should be done in such cases, sought a declaratory judgment against defendants to prevent not only future threatened suits by defendants on the same theory, but to prevent the present pending proceeding by defendants against plaintiffs on the same previously raised and abandoned issue.

Thus declaratory and injunctive relief is entirely appropriate here. As Professor Moore points out:

> "[T]he practice has developed of enforcing the res judicata effect of a judgment in appropriate situations by the equitable remedy of injuction - a remedy historically available for such purposes as restraining vexatious or harassing litigation ...." 1B Moore's Federal Practice ¶0.408[2], p. 957.

Similar declaratory and injunctive relief was sought and granted against the government in United States v. Willard Tablet Co., supra, and should be granted here.

POINT II

DEFENDANTS ARE BARRED FROM PROCEEDING AGAINST ALEVAIRE ON THE GROUNDS THAT IT MAY BE A FIXED COMBINATION DRUG WITHIN THE MEANING OF 21 C.F.R. 3.86 SINCE DEFENDANTS HAVE FAILED TO MEET THE JURISDICTIONAL REQUIREMENT OF "NEW INFORMATION" UPON WHICH TO BASE SUCH A PROCEEDING AS REQUIRED BY SECTION 505(e)(3) OF THE ACT

The second part of defendant's new proposal is based on the proposition that Alevaire may be a fixed combination drug within the meaning of 21 C.F.R. 3.86. This part of the proposal is invalid since the new Notice fails to specify, and defendants do not possess any "new information" which would indicate that Alevaire is a fixed combination drug and is ineffective as such.

1. Section 505(e)(3) of the Act, 21 U.S.C. §355(e)(3), Requires "New Information" to Support a Proceeding to Withdraw Approval of an NDA for Lack of Evidence of Effectiveness

The Federal Food, Drug, and Cosmetic Act is clear and unambiguous as to the basis required for initiation of a proceeding to withdraw approval of an NDA on the grounds of lack of evidence of effectiveness.

Section 505(e)(3) of the Act, 21 U.S.C. §355(e)(3), is as follows:

> "(e) The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds ... (3) on the basis of new in-

> formation before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof ..." (Emphasis added)(See Addendum A).

The legislative history is clear that Congress intended this language to require the Agency to have new information in addition to that available when the NDA was approved to support any new grounds for withdrawal of approval for lack of evidence of effectiveness. H.R. Rep. No. 2464, 87th Cong., 2d Sess. 8 (1962) stated:

> Under existing law, Section 505(e) provides that any application with respect to any new drug shall, after notice and opportunity for a hearing, be suspended if experience shows that the drug is unsafe or that the application contains any untrue statement of material fact. As amended by the committee, this section will, in addition, provide that approval of an application will be withdrawn if, on the basis of new evidence, evaluated with that originally submitted, the Secretary finds that the drug is not shown to be safe, or if new information, evaluated together with other evidence, indicates that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have. (Emphasis added)

The subsequent case law has made it abundantly clear that the statutory requirement of new information, and its parallel requirement of "new evidence" with respect to antibiotic certifications, are not mere surplusage in the statute,

but, rather, impose a burden upon the government to aduce substantial new evidence or information to support its proposal to withdraw NDA approval or antibiotic certifications. In Upjohn Co. v. Finch, 422 F.2d 944 (6th Cir. 1970), the Court stated:

> "It is further asserted by Upjohn that FDA could not apply the standard of substantial evidence to remove its products from the market because FDA had no new information or evidence with respect to the drugs in question at the time the certifications were revoked. The record demonstrates to the contrary. At the time he revoked the certifications, the Commissioner had before him the unanimous conclusion of thirty experts in antimicrobial therapy that the products in question are ineffective as fixed combinations. A number of other documents in the record, including some of the data submitted by Upjohn, reflect information which became available after these drugs had been certified by FDA and after enactment of the 1962 amendments ... We conclude from the record that FDA had additional information and evidence in 1969, when the certifications were revoked, which were not available to it in 1956 when Panalba, a fixed combination drug, was first certified as safe and effective." (422 F.2d at 951). (Emphasis added)

Thus the FDA in Upjohn was required to have and did have very substantial new information that the drugs there in question were "ineffective as fixed combinations." There, it had a report of the unanimous conclusion of thirty experts in the field involved that the drugs were "ineffective as fixed combinations." Here, as we shall subsequently show, the FDA has not a shred of new information to support its

proposal that Alevaire is "ineffective as a fixed combination." Bell v. Goddard, 366 F.2d 177 (7th Cir. 1966), and Pfizer, Inc. v. Richardson, 434 F.2d 536, 548 (2d Cir. 1970) also stand for the principle that the statutory requirements of "new evidence" and "new information" are necessary to sustain agency action.

This Congressional requirement of new information reflects the salutary public policy that one having received a license from a governmental agency is entitled to the lawful use of his rights thereunder, free from harrassment. Thus, while such rights are not irrevocable, the government may not arbitrarily or without statutory foundation withdraw such a license.

Approval of an NDA is, in effect, the grant of a license to market a drug, and Congress has provided that such approval may not be withdrawn arbitrarily without adequate reason. Thus, before the FDA can proceed to withdraw approval of an NDA based on lack of effectiveness, logic and precedent indicate that the statute requires that the Agency possess such "new information" before it may commence a withdrawal proceeding.

It is obvious that the Agency should not and does not have the power arbitrarily to decide to withdraw a previously approved NDA. When a drug has been approved and then

marketed for a number of years, there must be some new data or report that comes to the attention of the FDA before it may propose to remove that drug from the market. Logically, this is what Congress intended by the phrase in Section 505 (e)(3) and to serve this purpose, such "new information" must be present prior to the commencement of a withdrawal proceeding.

The requirement of "new information," therefore is a threshold requirement, which must be present before a withdrawal may be proposed. In fact, this is how the requirement has been treated by the Agency. In Upjohn, Bell and Pfizer, supra, the "new information" described by the courts and relied on by the Agency existed prior to the commencement of the proceedings and served as the condition precedent that caused the proceedings to be instituted in the first instance.

In fact, in the case at bar, it was the 1968 NAS-NRC report, which suggested there was a lack of substantial evidence that tyloxapol was more effective than water, which caused the Agency to commence the proceedings with regard to Alevaire. Plaintiffs never challenged the validity of that report to serve as the basis of the proceeding which then ensued, and it is obvious that defendants themselves have relied on similar panel reports to meet the requirements of "new information" in instituting withdrawal proceedings arising out of the NAS-NRC reviews.

Thus, the statute, logic and precedent all indicate that the "new information" requirement is one which must be met by FDA before proceeding to withdraw approval of an NDA.

2. Defendants Lack the Requisite "New Information" to Support their Proposal that Alevaire May Be A Fixed Combination Drug and Ineffective as Such

From 1952 in approving the initial NDA, until August, 1973, after it had written two withdrawal orders, the FDA always considered Alevaire to be a single entity drug. So too did the NAS-NRC panel. Then, suddenly, in the August 1973 withdrawal order which was issued just after the Supreme Court's decision in the Hynson case, the Agency was convinced that Alevaire was a fixed combination drug with four active ingredients, tyloxapol, water, sodium bicarbonate and glycerin. Now, in the new proposal, the FDA is not sure whether Alevaire is a single entity or a fixed combination drug, but, if it is the latter, the Agency feels it has three active ingredients, tyloxapol, water and sodium bicarbonate.

The fact is that the fixed combination theory as applied to Alevaire was manufactured out of whole cloth last summer and the FDA has absolutely no "new information" which even suggests that Alevaire is such a product.

Defendants' new proposal fails to specify any "new information" to support the fixed combination ground. However, the record below makes it clear that the only data

relied upon by defendants as allegedly constituting their "new information" to support the proposal that Alevaire is ineffective as a fixed combination drug is the 1968 NAS-NRC panel report. In their brief below, defendants stated:

> "In the case of Alevaire, such 'new information' is clearly provided by the results of the NAS-NRC study, and by the agency's re-evaluation of that and other data resulting in the conclusion that Alevaire is a fixed-combination drug." (A 122). (Defendants' repeated this assertion at the hearing. A 183-184).

That NAS-NRC report is obviously insufficient as a basis for the fixed combination proposal. The NAS-NRC report may have served as the "new information" required for the proceedings which began in 1968 in which Alevaire was considered a single entity drug. But that it cannot be utilized to provide any basis for the fixed combination proposal is clear from the face of the report itself, which makes no reference whatsoever to Alevaire as a fixed combination. To the contrary, as defendants concede, that report considered Alevaire to have a single active ingredient, tyloxapol (A 30). Moreover, since the NAS-NRC review panels themselves created the classification "ineffective as a fixed combination" (A 44) it is apparent that had the panel which reviewed Alevaire considered it to be such a drug, it would have classified it as such in its report.

The new proposal refers to statements allegedly made

"in package inserts used until 1970"* as indicating that Alevaire is a fixed combination product. (A 53). But this hardly constitutes the type of "intensive re-evaluation of clinical experience" referred to in Bell v. Goddard, supra, or even the short form reports issued by the NAS-NRC panels. Moreover, as defendants conceded on the prior appeal, those statements appeared in the labeling approved with the original NDA! (Respondents Brief in Dockets 73-1628 and 2481, p. 12; Addendum thereto, p. 2). Accordingly, the statements cannot constitute "new information" which was not before the Agency when the NDA was first approved.

We submit there is no "new information" to support the proposition that Alevaire is a fixed combination drug. We suggest that the proposition arose as an eleventh-hour attempt to avoid the impact of the Supreme Court decision in Weinberger v. Hynson, Westcott & Dunning, supra. As this Court stated:

> "On June 18, 1973, between the FDA termination of its March 2, 1973 order on June 14, 1973 and the issuance of its August 7, 1973 order, the Supreme Court decided Weinberger v. Hynson, Westcott & Dunning, 412 U.S. 609 (1973).
>
> * * *
>
> "Prior to the issuance of the August 7 order, the petitioners had submitted

*As usual, the Agency is factually inaccurate. The quoted labeling has not appeared in package inserts since the early 1960's.

> extensive evidence of Alevaire's effectiveness as a muco-evacuant to rebut the contention in the FDA notice that Alevaire was no more effective than water. Faced with the question of whether petitioners were entitled to a hearing on that issue under the Weinberger standards, the FDA then shifted its grounds to the new fixed combination theory in its August 7 order." (A 47-48).

In fact, the Court went on to say that "there is little in the record now before us to support the proposition that Alevaire is a fixed combination drug within the meaning of 21 C.F.R. 3.86 ..." (A 52)

By reason of the prior proceedings and the barrage of public pronouncements by the FDA that Alevaire is ineffective, the reputation of plaintiffs and their product have suffered irreparable damage, and sales of Alevaire have dropped over 63% since 1968 (A 67-68). Yet, the record demonstrates that thus far the Agency has been unable to substantiate its contentions and has been forced to withdraw two of its orders and has had the third one set aside.

Under such circumstances, and give the dubious genesis of the fixed combination theory, defendants should, at the least, be required to show that they meet the statutory requirements before they may force plaintiffs to submit to another withdrawal proceeding. As this Court stated, in any new proceeding the FDA "must follow the procedure required by the statute ..." (A 52).

POINT III

UNDER THE CIRCUMSTANCES AT BAR, THE DOCTRINE OF EXHAUSTION OF ADMINISTRATIVE REMEDIES DOES NOT APPLY

The sole ground of the decision below dismissing the Complaint was that plaintiffs have failed to exhaust their administrative remedies. We respectfully submit that, under the circumstances of this case, plaintiffs need not seek relief from the Agency in the first instance.

The exhaustion doctrine is not applicable where the administrative process has run its course and there is a clear-cut legal issue as to the effect of certain abandonments and concessions made by defendants before this Court during the appeals from those prior proceedings. Further, the Court may enjoin administrative action where, as here, it is apparent that the agency is proceeding without statutory authority.

1. Where Defendants Are Estopped From Again Raising a Previously Litigated and Abandoned Contention, Plaintiffs Need Not Exhaust their Administrative Remedies

As shown above, plaintiffs participated in full the administrative process from 1968 through 1973. They met each burden placed on them by the FDA and, in return, were met by

an Agency whose conduct "arbitrarily disregarded the requirements of the statute and its own regulations." (A 50).

When thwarted by the Agency, plaintiffs followed the appeal procedure under Section 505(h) of the Act, 21 U.S.C. §355(h). Even there, however, because of defendants' attempts to frustrate plaintiffs' appeals, it took, literally, three appeals for plaintiffs to achieve a hearing on the merits in this Court.

When the FDA was finally confronted before this Court with the clear prospect that, at the least, it would be required to hold an evidentiary hearing at which it would have to defend its criticisms of the Miller-Paez and Cohen studies, the Agency made a conscious and deliberate decision to avoid such prospect. It thus formally abandoned its criticisms of the two studies as being inadequate and uncontrolled.

Then, three months after this Court issued its decision and noted such abandonment, the Agency issued a new proposal adopting once again the exact position it has previously abandoned.

As shown above, this part of the new proposal should be barred by res judicata and related doctrines. The issues

are clear, fresh, and they are wholly legal in nature.

Nevertheless, the decision of the District Court below states that:

> "the proper procedure is for the plaintiffs to raise this defense in the administrative proceedings and then have the agency determination on this issue (should it be contrary to plaintiffs' claim) reviewed on the appeal to the court of appeals from whatever adverse final decision the FDA may make with respect to the withdrawal proceedings." (A 206).

We cannot agree. To require exhaustion of remedies here is to thwart the rationale behind the doctrine of res judicata. In the first instance, it will be futile to submit this issue to the Agency. By the very issuance of the new proposal, and by their unequivocal posture in this litigation, defendants have made it very clear that they do not consider themselves barred from relitigating the previously abandoned issue. As stated by defendants below, it is their contention that:

> "there is, however, no merit to the claim that the agency is barred from proceeding on the single-entity theory by the doctrine of res judicata or collateral estoppel ..." (A 121).

In sum, no relief can be expected on this point within the Agency and under such circumstances exhaustion is not required:

> "The circumstances of the present case call into play another of the most obvious exceptions to the exhaustion requirement - the situation where the effort to proceed formally with ... administrative remedies would be wholly futile." Glover v. St. Louis - San Francisco R. Co., 393 U.S. 324, 330 (1969); cf. Diapulse Corp. of America v. Food & Drug Administration, 500 F.2d 75, 77-78 (2d Cir. 1974)

Moreover, there is no reason to submit this issue to the Agency. The purpose of the exhaustion doctrine is to allow an agency to exercise its particular expertise. McKart v. United States, 395 U.S. 185, 194 (1969). But, what is at stake at bar is the legal effect of proceedings before this Court which culminated in a decision last May, and the FDA has no special expertise to bring to bear on these legal issues. Where the matter to be decided is strictly legal, and does not involve the special competence of the Agency, there is no reason to apply the exhaustion doctrine. The matter is simply not one for Agency determination and the rationale behind the exhaustion doctrine does not apply. Diapulse Corp. of Am. v. Food & Drug Administration, supra at 78; American Nursing Home Ass'n v. Cost of Living Council, 497 F.2d 909, 913 (Em. Ct. App. 1974).

Moreover, while the exhaustion doctrine is not relevant under these facts, the vitality of the doctrine of res judicata is directly involved. If plaintiffs are forced to submit to the administrative process, it may be years before they are able to return to this Court to seek a ruling on the issue of res judicata. The last proceedings, without an evidentiary hearing, took over five years. Even if a hearing is granted in these proceedings, a good deal of time will pass before a final order is reached and, of course,

plaintiffs will be required to litigate the very issue they claim is not subject to relitigation.

Accordingly, the ruling below that plaintiffs must exhaust their administrative remedies on this issue will substantially emasculate the docrtine of res judicata. Plaintiffs will have received no relief from harassment and there will be little vitality in that equitable doctrine if, on appeal from a full hearing on the merits, this Court holds that plaintiffs need not have participated therein in the first place.

The decision below further suggests that review of this issue should follow the normal course created by the Congress and await appeal from a final order pursuant to 21 U.S.C. §355(h). (A 204). We submit, however, that a decision on the merits by this Court at this time will reinforce, rather than circumvent, the Congressional scheme. Under the facts at bar, plaintiffs have already participated in the administrative process and this Court has already rendered its decision on review. If the Agency is allowed to avoid the effect of that decision, then this Court's statutory role as final arbiter will have been undermined. Indeed, to adopt the view that exhaustion is required is to open the possiblity that an agency could always avoid the effect of final rulings simply by commencing a new

proceeding on the same ground and, when challenged, argue that judicial review must await a final order. Moreover, the fact that review is available at a later date does not bar a decision at this time. Cf., American Communications Ass'n v. United States, 298 F.2d 648, 650 (2d Cir. 1962).

For all these reasons, the exhaustion doctrine should not apply under the circumstances at bar. The cases cited in the opinion below are not persuasive. Petro v. Bakely, 353 F.2d 511 (3d Cir. 1965), was a negligence action involving no administrative agency, where defendant moved in the district court to dismiss the action as barred by res judicata. The motion was denied and the appeal was "dismissed for want of jurisdiction", 353 F.2d at 512, since the order denying the motion was not a final one pursuant to 28 U.S.C. §§ 1291, 1292.

It does not appear that the defendant in Petro sought certification pursuant to 28 U.S.C. §1292. Presumably, a close question of res judicata which could be dispositive of a major part of the litigation would appropriately be certified. Cf., Atlantic City Electric Co. v. General Electric Co., 207 F.Supp. 613 (S.D.N.Y. 1969), aff'd 312 F.2d 236 (2d Cir. 1962), cert. denied 373 U.S. 909 (1963), where a question

as to the applicable statute of limitations was certified. Here, plaintiffs are seeking what defendant in Petro received, a decision on the merits, at the outset, on their res judicata claim.

The decision below also relied on SEC v. Otis & Co., 338 U.S. 843 (1949) (per curiam), rev'g, Otis & Co. v. S.E.C., 176 F.2d 34 (D.C. Cir. 1949). The per curiam reversal on the peculiar facts in Otis is not controlling under the circumstances at bar. In Otis, the SEC had commenced a "private investigation" during the course of which it had subpoenaed two attorneys. The attorneys refused to answer certain questions on the grounds of attorney-client privilege and the SEC filed a suit to compel their testimony on the grounds that the privilege did not apply to consultations concerning the perpetration of a fraud. The district court ruled against the Commission on the grounds that the SEC had not made "the requisite prima facie showing of fraud to pierce the attorney-client privilege." 176 F.2d at 36.

While the case was pending in the district court, the SEC commenced a formal adjudicatory proceeding arising out of the same factual background. After the district court had ruled on the privilege point, Otis sued the SEC in the district court to enjoin the proceeding as barred by res judicata. The district court dismissed the complaint but the

court of appeals reversed and remanded the case to the district court with instructions to give the SEC "an opportunity to answer and to deny the allegation that no additional evidence concerning Eaton's collusion will be introduced at its new hearing, and so be relieved of the bar of res judicata." 176 F.2d at 44.

The Supreme Court granted certiorari and then reversed the Court of Appeals in a per curiam decision, citing Myers v. Bethlehem Shipbuilding Co., 303 U.S. 41 (1938), Macaulay v. Waterman S.S. Corp., 327 U.S. 540 (1946), and Federal Power Commission v. Arkansas Power & Light Co., 330 U.S. 802 (1947).

Given the unique facts in Otis, the case does not stand as a bar to the consideration by this Court of the res judicata issue. In Otis, the SEC was commencing an adjudicatory proceeding and the decision relied on as a bar had come in a subpoena enforcement proceeding deriving from a "private" investigation. Even the court of appeals recognized that the Commission should have the right to show new or additional evidence to avoid res judicata effect. It is quite conceivable that the Supreme Court felt that a bar of the entire proceeding on those facts was simply too drastic and that the Commission should be given the opportunity in its own proceeding to show independent evidence of fraud.

Indeed, the Supreme Court might well have taken into account the companion decision of the district court in Otis & Co. v. National Ass'n of Securities Dealers, 84 F.Supp. 395 (D.D.C. 1949) where the court had indicated that despite the exhaustion doctrine, it would take immediate cognizance of any attempt by the Commission prior to final review to force a divulgence of privileged material:

> "[I]t is equally apparent that no final action adverse to the plaintiffs can be effective until they have had opportunity to apply to a Court for a stay of such action. If the plaintiffs could be coerced, either by the Association or the Securities and Exchange Commission, in divulging the communications which have held to be within the attorney-client privilege short of a judicial determination that the plaintiffs could be legally required in the circumstances to divulge such confidential communications, I would not have the slightest doubt that this Court could and should undertake a determination of the rights of the parties with respect to these questions; but that is not the case." 84 F.Supp. at 398.

Otis, then, presents a far different factual picture from the case at bar. The equitable compulsion to apply the doctrine of res judicata was far less there, where it was not at all clear that Otis' rights would be infringed, than here, where the relitigation will be of the exact same issue in the same kind of proceeding. Also, the rationale in favor of the

exhaustion doctrine was stronger there, where no adjudicatory proceeding had been conducted, than here, where the parties have already gone through the administrative procedure contemplated by statute.*

Moreover, none of the cases cited by the Supreme Court in its per curiam reversal in Otis involved issues of res judicata. Myers v. Bethlehem Shipbuilding Corp., supra, cited therein and heavily relied on by defendants in this case, involved a traditional ground for application of the exhaustion doctrine, namely, giving an agency initial leeway to determine whether it has jurisdiction over the subject matter. Similar issues were involved in Macauley v. Waterman S.S. Corp., supra, and Federal Power Commission v. Arkansas Power & Light Co., supra. The rationale of those decisions is to allow the agency to exercise its expertise in determining whether it may proceed in the first instance. That rationale does not apply here where the issue concerns the legal effect of proceedings before this Court and where plaintiffs do not challenge the basic jurisdiction of the FDA to conduct withdrawal proceedings. Elmo Division of Drive-X Co v. Dixon, 348 F.2d 342, 344 (D.C. Cir. 1965).

*Coca-Cola Co. v. FTC, 475 F.2d 299 (5th Cir. 1973), cert. denied 414 U.S. 877 (1973), also cited in the decision below, provides no precedent for requiring exhaustion here. That case involved the reviewability of motions to intervene in pending agency proceedings. There was no clear res judicata issue. Rather, the plaintiffs speculated that there might be res judicata problems in the future unless intervention was granted.

In addition, Otis and Myers are older cases which have been erroded over the years. As this Court noted in Bristol-Myers v. FTC, 469 F.2d 1116, 1118 (2d Cir. 1972), "the administrative exhaustion doctrine is less an inflexible command than a general guideline." While the exceptions to the doctrines are not clear cut and perhaps must be determined on a case by case basis, this Court recently indicated that:

> "one can find 'final agency action for which there is no other adequate remedy in a court' if an agency refuses to dismiss a proceeding that is plainly beyond its jurisdiction as a matter of law or is being conducted in a manner that cannot result in a valid order." Pepsico, Inc. v. F.T.C., 472 F.2d 179, 187 (2d Cir. 1972), cert. denied 414 U.S. 876 (1973)

Here, since res judicata applies, the FDA can issue no valid final order, and it is appropriate for this Court to rule at this time.

Similarly, in Elmo Division of Drive-X Co. v. Dixon, supra, judicial intervention was justified since if plaintiff was forced to participate in an improper proceeding it would have no adequate relief on appeal and since the FTC had no special expertise to exercise on the procedural question presented.

Accordingly, the exhaustion doctrine is not applicable to the instant case and, in any event, should not be

applied since the countervailing considerations of effective relief for plaintiffs and enforcement of the decision of this Court outweigh any factors favoring exhaustion.

2. Where Part of Defendants' Proposal Lacks the "New Information" Required By Statute, Plaintiffs Need Not Exhaust Their Administrative Remedies

As shown above, the Act required that the FDA possess "new information" in order to maintain a withdrawal proceeding and none is present insofar as the "fixed combination" part of the new proposal is concerned.

Where the Agency is proceeding in violation of its statutory authority, there is no need for plaintiffs to exhaust their administrative remedies. Leedom v. Kyne, 358 U.S. 184 (1958); Elmo Division of Drive-X Co. v. Dixon, supra; cf. Pepsico, Inc. v. F.T.C., supra.

Here, the issue is one of statutory construction concerning the requirement of "new information". In that regard, this case closely resembles Jewell Companies, Inc. v. Federal Trade Commission, 432 F.2d 1155 (7th Cir. 1970), where it was held that a district court could enjoin an FTC proceeding while it decided a question of statutory construction concering the scope of the agency's discretion. Cf., California ex. rel. Christensen v. F.T.C., ____ F.Supp. ____, CCH TRADE REG. REP. ¶75,328 (N.D. Cal., October 29, 1974).

3. Where Defendants' Proposal Violates Plaintiffs' Constitutional Right to Due Process of Law, Plaintiffs Need Not Exhaust Their Administrative Remedies

By seeking again to withdraw the NDA's for Alevaire on grounds previously raised and abandoned as erroneous, defendants are acting arbitrarily to harass plaintiffs and to damage plaintiffs' reputation and that of their product. The same damage arises from defendants' attempt to proceed against Alevaire on the fixed combination ground in the absence of the "new information" required by the Act. Since the agency is acting arbitrarily and without authority, and in so doing is damaging plaintiffs' valuable property rights in their license and product, it is violating the Due Process guaranteed plaintiffs by the Fifth Amendment.

Where plaintiffs' "assertion of constitutional right is not transparently frivilous," the exhaustion doctrine does not apply. Fay v. Douds, 172 F.2d 720, 723 (2d Cir. 1949); Amos Treat & Co. v. S.E.C., 306 F.2d 260 (D.C. Cir. 1962); Council 19, Am. Fed. of State, Co. & Mun. Emp. v. N.L.R.B., 296 F.Supp. 1100 (N.D. Ill. 1968); Lehigh Portland Cement Co. v. FTC, 291 F.Supp. 628 (E.D. Va. 1968), aff'd 416 F.2d 971 (4th Cir. 1968). The Court has jurisdiction and should dispose of the substantive issues raised.

CONCLUSION

Plaintiffs should not be required to participate in an unlawful proceeding. They are part of what the Supreme Court has recognized to be a "sensitive industry in which public confidence in their drug products is especially important," Abbott Laboratories v. Gardner, 387 U.S. 136, 153 (1967), and pharmaceutical sales, once lost, are difficult if not impossible to recoup "because of a permanent loss of medical confidence and a permanent loss of sales to competing products," American Home Products Corp. v. Finch, 303 F.Supp. 448, 452 (D. Del. 1969). The reputation of plaintiffs and the reputation and sales of Alevaire have suffered enough during the course of the prior proceedings which have been shown to be unjustified scientifically and legally. Since there is a strong public interest "in protecting the drugs that are useful in the prevention, control, or treatment of illness," Weinberger v. Hynson, Westcott & Dunning, Inc., supra at 639 (Powell, J., concurring), this Court should enjoin the FDA from proceeding in violation of the Act and should ensure that any future proceedings with regard to Alevaire be in accordance with law.

For the reasons set forth above, the decision of the District Court denying an injunction and dismissing the Complaint for failure to exhaust administrative remedies should be reversed and remanded to the District Court with instructions to enter judgment as prayed for in the Complaint.

Respectfully submitted,

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ADDENDUM A

Section 505e, Federal Food, Drug & Cosmetic Act, 21 U.S.C. §355e

(e) The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) that the application contains any untrue statement of a material fact: *Provided*. That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (j) or to comply with the notice requirements of section 510(j)(2), or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

Carol Cleaver (Ret.)
November 26, 1974

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